

SUPPOSITORY BASES

Classification of suppository bases

1. *Fatty bases* – they melt at body temperature.
2. *Water-soluble or water miscible base* – they dissolve or disperse in rectal secretions.
3. *Emulsifying bases* – they emulsifies small amount of aqueous solution of drug.

FATTY BASES

Example: Theobroma oil (Cocoa butter), Synthetic fats.

Theobroma oil (Cocoa butter)

- It is a yellowish-white solid having chocolate flavor.
- It is a mixture of glyceryl esters of stearic, palmitic, oleic and other fatty acids.

Advantages:

- (a) A melting point range of 30 to 36 °C; hence it is solid at normal room temperatures but melts in the body.
- (b) Ready liquefaction on warming and rapid setting on cooling.
- (c) Miscibility with many ingredients.
- (d) Blandness i.e. does not produce irritation.

Disadvantages:(a) Polymorphism

Cocoa butter has three polymorphs α -crystals (unstable, m.p. 20°C), β -crystals (stable, m.p. 36°C) and γ -crystals (unstable, 15°C).

When melted and cooled it solidifies in different crystalline forms, depending on the temperature of melting, rate of cooling and size of the mass. If melted below 36°C and slowly cooled it forms stable β -crystals with normal melting point, but if over-heated it may produce, on cooling, unstable γ -crystals, which melt at about 15°C, or α -crystals, melting at about 20°C. These unstable forms eventually return to the stable condition but this may take several days and meanwhile, the suppositories may not set at room temperature or, if set by cooling, may remelt in the warmth of the patient's home.

This lowering of the solidification point can also lead to sedimentation of suspended solids. Consequently, great care must be taken to avoid over-heating the base when making theobroma oil suppositories.

(b) Adherence to mould

Because theobroma oil does not contract enough on cooling to loosen the suppositories in the mould, sticking may occur, particularly if the mould is worn. This is prevented by lubricating the mould before use.

(c) Softening point too low for hot climates

To raise the softening point, whit beeswax may be added to theobroma oil suppositories intended for use in tropical and subtropical countries.

(d) Melting point reduced by soluble ingredients

Substances, such as chloral hydrate, that dissolve in theobroma oil, may lower its melting point to such an extent that the suppositories are too soft for use. To restore the melting point, a controlled amount of white beeswax may be added.

(e) Slow deterioration during storage

This is due to oxidation of the unsaturated glycerides.

(f) Poor water absorbing capacity

This fault can be improved by the addition of emulsifying agents.

(g) Leakage from the body

Sometimes melted base escapes from the rectum or vagina. This is most troublesome with pessaries because of their larger size, and therefore, these are rarely made with theobroma oil.

(h) Relatively high cost**Synthetic fats**

As a substitute of theobroma oil a number of hydrogenated oils, e.g. hydrogenated edible oil, arachis oil, coconut oil, palm kernel oil, stearic and a mixture of oleic and stearic acids are recommended.

[N.B. Synthetic suppositories bases are by hydrogenation and subsequent heat treatment of vegetable oils such as palm oil and arachis oil. The oils are generally esters of unsaturated fatty acids. Hydrogenation saturates the unsaturated fatty acids and heat treatment splits some of the triglycerides into fatty acids and partial esters (mono- and di-glycerides).]

Advantages of these synthetic fats over theobroma oil:

1. Their solidifying points are unaffected by overheating.
2. They have good resistance to oxidation because their unsaturated fatty acids have been reduced.
3. Their emulsifying and water absorbing capacities are good. [They usually contain a proportion of partial glycerides some of which, e.g. glyceryl monostearate, are w/o emulsifying agents and, therefore, their emulsifying and water absorbing capacity are good.
4. No mould lubricant is required because they contract significantly on cooling.

5. They produce colorless, odourless and elegant suppositories.

Disadvantages:

1. They should not be cooled in refrigerator because they become brittle if cooled quickly. Certain additives e.g. 0.05 % polysorbate80, help to correct this fault.
2. They are more fluid than theobroma oil when melted and at this stage sedimentation rate is greater. Thickeners such as magnesium stearate, bentonite and colloidal silicon dioxide, may be added to reduce this.

WATER SOLUBLE AND WATER MISCIBLE BASES

Glycero-Gelatin base

- This is a mixture of glycerol and water made into a stiff jelly by adding gelatin.
 - It is used for the preparation of jellies, suppositories and pessaries. The stiffness of the mass depends upon the proportion of gelatin used which is adjusted according to its use.
 - The base being hydrophilic in nature, slowly dissolves in the aqueous secretions and provide a slow continuous release of medicament. Glycerogelatin base is well suited for suppositories containing belladonna extract, boric acid, chloral hydrate, bromides, iodides, iodoform, opium, etc.
 - Depending upon the compatibility of the drugs used a suitable type of gelatin is selected for the purpose. Two types of gelatins are used as suppository base
- (i) **Type-A or Pharmagel-A** which is made by acid hydrolysis (has isoelectric point between 7 to 9 and on the acid side of the range behaves as a cationic agent, being most effective at pH 7 to 8.) is used for acidic drugs.
 - (ii) **Type-B or Pharmagel-B** which is prepared by alkaline hydrolysis (having an isoelectric point between 4.7 to 5 and on the alkaline side of the range behaves as an anionic agent, being most effective at pH 7 to 8) is used for alkaline drugs

Disadvantages:

Glycerogelatin base suppositories are less commonly used than the fatty base suppositories because:

- (i) Glycerol has laxative action.
- (ii) They are more difficult to prepare and handle.
- (iii) Their solution time depends on the content and quality of the gelatin and the age of the base.
- (iv) They are hygroscopic, hence must be carefully stored.
- (v) Gelatin is incompatible with drugs those precipitate with the protein e.g. tannic acid, ferric chloride, gallic acid, etc.

Soap-Glycerin Suppositories

- In this case gelatin and curd soap or sodium stearate which makes the glycerin sufficiently hard for suppositories and a large quantity of glycerin up to 95% of the mass can be incorporated.
- Further the soap helps in the evacuation of glycerin.
- The soap glycerin suppositories have the disadvantage that they are very hygroscopic, therefore they must be protected from atmosphere and wrapped in waxed paper or tin foil.

Polyethylene glycol bases / Macrogol bases (Carbowaxes)

Depending on their molecular weight they are available in different physical forms.

Examples of Macrogol bases:

	I	II	III	IV
Macrogol 400	-	-	20	-
Macrogol 1000	-	-	-	75
Macrogol 1540	-	33	33	-
Macrogol 4000	33	-	-	25
Macrogol 6000	47	47	47	-
Water	20	20	-	-

By choosing a suitable combination a suppository base with the desired characteristics can be prepared.

Advantages:

1. The mixtures generally have a melting point above 42°C, hence, does not require cool storage and they are satisfactory for use in hot climate.
2. Because of the high melting point they do not melt in the body cavity, rather they gradually dissolve and disperse, releasing the drug slowly.
3. They do not stick to the wall of the mould since they contract significantly on cooling.

EMULSIFYING BASES

These are synthetic bases and a number of proprietary bases of very good quality are available, few of which are described below:

Witepsol

They consist of triglycerides of saturated vegetable acids (chain length C12 to C18) with varying proportions of partial esters.

Massa Esterium

This is another range of bases, consisting of a mixture of di-, tri- and mono- glycerides of saturated fatty acids with chain lengths of C11 to C17.

Massuppol

It consists of glyceryl esters mainly of lauric acid, to which a small amount of glyceryl monostearate has been added to improve its water absorbing capacity.

Advantages of these bases over cocoa butter:

1. Over heating does not alter the physical characteristics.
2. They do not stick to the mould. They do not require previous lubrication of the mould
3. They solidify rapidly.
4. They are less liable to get rancid.
5. They can absorb fairly large amount of aqueous liquids.